

In This Issue:

**Levodopa and the Progression of PD
Clinical Trials for Later Stage PD
Apokyn Used for PD
Low Calorie Diets and PD in Monkeys
Aging America
Happenings from the Houston PADRECC**

**Rivastigmine and PD Dementia
“Hedgehog, Gli-1, and Nurr-1”
DBS After Pallidotomy
Coffee, Gender and PD
News...In a Minute
Houston PADRECC Contact Information**

Levodopa and the Progression of PD

This randomized, double-blind, placebo-controlled trial, conducted by the Parkinson Study Group, evaluated 361 patients with early PD who were assigned to either one of three daily doses of carbidopa-levodopa or a matching placebo for 40 weeks. The primary outcomes were a change in scores of the UPDRS and neuroimaging studies to assess striatal dopamine-transporter density. Results suggested that the severity of PD symptoms increased more in the placebo groups than in all the groups receiving levodopa. Those taking the highest doses of L-dopa did the best. The neuroimaging data suggested that levodopa accelerated the loss of nigrostriatal dopamine nerve terminals, but those changes did not worsen the symptoms of PD. The potential long-term effects of levodopa on PD remain uncertain.

<http://content.nejm.org/cgi/content/short/351/24/2498/>

Rivastigmine and PD Dementia

410 PD patients completed a 24-week placebo-controlled study testing rivastigmine (Exelon) for dementia associated with PD. This was the first large-scale trial assessing the efficacy and safety of an Alzheimer's disease (AD) drug as a treatment for PD dementia. Although the changes were modest, patients treated with 3-12 mg daily of rivastigmine showed statistically significant improvement on memory, concentration, and behavioral changes. The outcomes were similar to those reported for Alzheimer's disease (AD). Motor conditions did not worsen in the treated patients, but mild to moderate nausea and vomiting were observed.

<http://nejm.org/cgi/content/abstract/351/24/2509>

Clinical Trials for Later Stage PD

Mid to later stage PD patients may have the opportunity of being considered for a Phase I/II clinical trial (safety of increasing doses) using Avigen's AV201. The purpose of AV201 is to restore and extend the therapeutic effectiveness of levodopa, a precursor to dopamine. AV201 is an AAV vector containing the gene for AADC, a protein that converts levodopa to dopamine in the brain. It is delivered directly to the striatum, the part of the brain that requires dopamine to control movement. As PD progresses, AADC becomes less available and less efficacious in producing dopamine in the brain. Studies in animal models of PD have demonstrated AADC expression for up to 5 years after a single administration of the gene, along with continued therapeutic benefit. http://biz.yahoo.com/prnews/041216/sfth045_1.html

“Hedgehog, Gli-1, and Nurr-1”

Researchers have found that two specific proteins - “sonic Hedgehog (Shh)” and “Gli-1” prevented progressive deterioration of the nerve cells that causes PD in genetically engineered laboratory rats. Those cells treated with “Nurr-1”, a protein needed to produce substantia nigra neurons in the brain, were not protected. The dopaminergic growth factor “GDNF” was used as a positive control. The viral transfer of sonic Hedgehog and Gli-1 proteins, which are involved in

early brain development but no longer present in the adult brain, may prevent cell death by selectively protecting dopaminergic cell bodies from a specific neurotoxic insult.
Molecular Genetics (DOI:10.1016/j.ymthe.2004.05.021)

Apokyn Used for PD

The FDA has approved a new PD drug, Apokyn (apomorphine), as an injectable (subcutaneous) drug for the acute treatment of hypomobility in patients with advanced PD. Apomorphine must be taken with an antiemetic drug and must not be taken with 5HT3 antagonists due to the possibility of hypotensive episodes. Apokyn is available at the Houston PADRECC.
<<http://www.fda.gov/bbs/topics/ANSWERS/2004/ANS01284.html>>

DBS After Pallidotomy

Researchers found that bilateral STN DBS is safe and efficacious in improving motor symptoms in patients with prior pallidotomy. Changes in UPDRS Motor and Activities of Daily Living scores, medication requirements, and dyskinesias were measured and compared with patients without a prior pallidotomy. Significant differences in reduction of UPDRS motor scores were noted for those with prior pallidotomy, but less change in dyskinesia duration and disability scores. There were no side-to-side differences clinically or in the STN electrophysiological readings. The first author, Dr. Kellner-Fisman, is a neurologist at the Philadelphia VA PADRECC. <<http://www3.interscience.wiley.com/cgi-bin/abstract/108565260/ABSTRACT>>

Low Calorie Diets and PD in Monkeys

A team from the NIA examined whether a long-term reduction in caloric intake protected rhesus monkeys from developing PD. For six months, monkeys received a diet with 30% fewer calories than the control diet. The monkeys were then injected with a toxin that caused PD-like symptoms. The calorie-restricted monkeys showed better control over movement and higher levels of dopamine and GDNF in their brains. Calorie restriction may stimulate the production of neurotrophic factors by causing a mild stress response in the brain that responds by producing protective proteins against neurodegenerative diseases.
<<http://www.pnas.org/cgi/content/abstract/0405831102v1?maxtoshow>>

Coffee, Gender, and PD

The possibility of an interaction between caffeine and estrogen in modulating the risk of PD may provide new clues on their mechanism of action. The risk of PD has been found to be reduced in men who regularly consume caffeine, but not among non-estrogen treated postmenopausal women. The results obtained from the Cancer Prevention Study II Cohort suggest that estrogen has potent but incompletely understood effects on the nigrostriatal dopaminergic system and is a competitive inhibitor of caffeine metabolism. The researchers caution that these results indirectly supports a neuroprotective mechanism of caffeine but further study is needed.
<http://www.ingentaconnect.com/content/oup/aje/2004/00000160/00000010/art00977;jsessionid=979diihk8aqb3.victoria>

Aging America

A recent publication of The National Governors Association (NGA) Center for Best Practices focuses on aging America. The report, "Measuring the Years: State Aging Trends and Indicators" reports these findings:

- States are expected to experience a dramatic shortfall in longterm care workers.
- Excluding home equity, seniors' median annual income totals only \$23,369.
- State health and aging officials now consider chronic disease prevention and control a higher priority than access to health care or prescription drugs.

- 50% of seniors live with at least 2 chronic illnesses, 80% experience at least 1.

<http://www.nga.org/cda/files/04DATABOOK01.PDF>

News ...In a Minute

a. Alzheimer's Report Available

The 2003 Progress Report on Alzheimer's Disease offers a comprehensive overview of recent advances in government-supported AD research. For the pdf format, look up:

www.alzheimers.org/pr03/index.asp <<http://www.alzheimers.org/pr03/index.asp>>

b. NIH Sets up PD Data Center

The NIH has selected the University of Rochester (UR) as home for the new Parkinson's Disease Data and Organizing Center. UR's medical center already is home to the Parkinson Study Group. The new center will set standards for evaluating and sharing data from 15 PD NIH centers.

<http://www.democratandchronicle.com/apps/pbcs.dll/search>

c. Upcoming National Events

March 5-8, 2005, 9th International Congress of Parkinson's Disease and Movement Disorders.

The New Orleans Marriott, New Orleans, LA. Web site: www.movementdisorders.org

April 9-16, 2005, American Academy of Neurology 57th Annual Meeting. Miami, FL. Web site:

www.aan.com <<http://www.aan.com>>

d. Revised NPF Booklet

The National Parkinson Foundation has revised a previous publication "Activities of Daily Living: Practical Pointers for Parkinson Disease." The publication is available through their website: www.parkinson.org (library publications/online library section).

Happenings at the Houston PADRECC

PADRECC Seminar January 25, 2005 "Epidemiology in the 21st Century." Donna White, PhD., presenter.

April 30, 2005 PADRECC Presents: "A Wellness Fair for Individuals with Parkinson's Disease and their Families," Houston, TX. Location TBA.

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